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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,676	11/28/2000	Zurit Levine	ILEX:032	9311

20999 7590 02/28/2003

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EXAMINER

MARSCHER, ARDIN H

ART UNIT PAPER NUMBER

1631

DATE MAILED: 02/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/724,676

Applicant(s)

LEVINE ET AL.

Examiner

Ardin Marschel

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on 28 October 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-85 is/are pending in the application.
- 4a) Of the above claim(s) 1,2 and 4-85 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 3 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-85 are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

Applicant's election with traverse of Group II (claim 3) and SEQ ID NO: 70493 in Paper No. 9, filed 10/28/02, is acknowledged. The traversal is on the ground(s) that a search for nucleic acid sequences is likely to be coextensive, that PCT Administrative Instructions indicates that Unity of Invention exists between inventions such as Groups I and II, and that Groups classified in class 530, subclass 300, should be searched with subject matter classed in class 435, subclass 7.1. This is not found persuasive because searching for a chemical structure such as an amino acid sequence is clearly a different chemical from a nucleic acid sequence. As described in the previous Office action, these different chemicals are non-overlapping chemicals and therefore the search for each is independent. Applicants' arguments have not resolved this different chemical structure issue and thus the allegation that a search for an amino acid sequence and a nucleic acid sequence is coextensive conflicts with the fact that these are different chemicals and thus require searching over different disclosure thus well documenting the undue search burden if they were to be searched together. This argument is therefore non-persuasive. The argument regarding PCT Unity of Invention is moot as the instant application is not a PCT application, nor is it a 371 filing from a PCT application. Applicants' argument regarding searching Groups classified in Class 530, subclass 300, versus classified in Class 435, subclass 7.1, is also non-

persuasive for the reason that the previous Office action set forth the restriction requirement between subject matter, only listing class/subclass information for merely indicating that these separate class/subclass categories exists for different Groups of inventions. Thus, since this argument is not directed to the distinct subject matter basis for the restriction between invention Groups as set forth in the previous Office Action, mailed 4/29/02, this argument is also non-persuasive as not being directed to the basis for the restriction requirement.

The requirement is still deemed proper and is therefore made FINAL.

#### TITLE

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The present title is directed to variants of alternative splicing which lacks indicating that the elected subject matter under examination is directed to an amino acid sequence.

#### LACK OF UTILITY

The pending claims have been reviewed in light of the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. 112, first paragraph, "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1092-1111, Friday, January 5, 2001.

The examiner is using the following definitions in evaluating the claims for utility.

"Specific" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention.

"Substantial" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

"Credible" - Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the applicant's assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

"Well-established" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claim 3 is rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by either specific and/or substantial utility or a well established utility.

The claimed amino acid sequence is not supported by a specific asserted utility because the disclosed uses of these compositions are not specific and are generally applicable to any amino acid sequence. The specification summarizes modern biotechnology generally but never connects the specifically elected sequence to any particular or specific utility. This wishlist desire for a utility for the claimed sequences falls short of a readily available utility. Similarly, protein may be used for detection of expression, antibody production, Western blots, etc. These are non-specific uses that are applicable to proteins in general and not particular or specific to the amino acid sequence being claimed.

Further, the claimed amino acid sequence is not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. A protein could be used in conducting research to functionally characterize the protein. The need for such research clearly indicates that the protein and/or its function is not disclosed as to a currently available or substantial utility. A starting material that can only be used to produce a final product does not have substantial

asserted utility in those instances where the final product is not supported by a specific and substantial utility. In this case none of the amino acid sequences that may be produced as final products have identified specific and substantial utilities. The research contemplated by applicant(s) to characterize potential protein products, especially their biological activities, does not constitute a specific and substantial utility. Identifying and studying the properties of a protein itself or the mechanisms in which the protein is involved does not define a "real world" context or use. Similarly, the other listed and asserted utilities in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds. Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility has not been assessed. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the amino acid sequence such that another non-asserted utility would be well established for the compounds.

It is noted that applicants apparently have identified the claimed sequence as being a kinase via sequence analysis. Absent actual evidence, one skilled in the art would have reason to doubt that sequence similarity alone would reasonably support the assertion that the biological activity of the claimed subject

matter would be the same as that of a similar sequence. Furthermore, it is unclear whether the similar sequence identified in the prior art has actually been tested for the biological activity or whether this also is an asserted biological activity based upon sequence similarity to yet a different sequence. Note that it would have been well known in the art that sequence similarity does not reliably correlate to structural similarity and that structural similarity does not reliably result in similar or identical biological activities. For example, it would have been well known that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. In the absence of factual evidence characterizing the structural and functional components of the biomolecule, the effects of these changes are largely unpredictable as to which ones will have a significant effect and which ones will be silent mutations having no effect. Several publications document the unpredictability of the relationship between sequence, structure, and function, although it is acknowledged that certain specific sequences have been found to be conserved in biomolecules having related function following a significant amount of further research. See Attwood (Science, 290:471-473, 2000); Lopez et al. (Molecular Microbiology, 32: 886-891, 1999); Gerhold et al. (BioEssays, 18(12):973-981, 1996); Wells et al. (Journal of Leukocyte Biology, 61(5):545-550, 1997); and Russell et al.



(Journal of Molecular Biology, 244:332-350, 1994).

#### LACK OF ENABLEMENT

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 3 is also rejected under 35 U.S.C. § 112, first paragraph. Due to a lack of either an art recognized or alleged well established utility, the instant invention has been rejected due to also lacking the required combination of a specific, substantial, and credible utility. Although it may be credible that the elected amino acid sequence affects and or is involved in biological function(s), the lack of a specific and substantial utility, as explained above, sufficiently supports this rejection. In summary, since the claimed invention is not supported by the combination of a specific, substantial, and credible utility, or, alternatively, a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

Claim 3 is rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling (subject to the above noted lack of enablement) for SEQ ID NO: 70,493, does not reasonably provide enablement for homologues defined as having

sequence additions, deletions, or replaced or chemically modified amino acids in the region that differs from the "original amino acid sequence". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

In order to evaluate the homologues as cited in part (ii) of claim 3 a region which differs from the "original amino acid sequence" is required. Applicants have not set forth what this

"original amino acid sequence" is for comparison to SEQ ID NO: 70,493. This total lack of guidance regarding this "original amino acid sequence" leaves someone of skill in the art to undue experimentation in order to determine what this is as any of a myriad of sequences may be the "original amino acid sequence" due to a lack of limitation in instant claim 3 regarding how many additions, deletions, replacements, or modifications of amino acids may be present in a splice variant.

#### LACK OF WRITTEN DESCRIPTION

Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses SEQ ID NO: 70,493. SEQ ID No: 70,493 per se meets the written description provision of 35 USC 112, first paragraph. However, claim 3 is directed to encompass homologues of sequences of SEQ ID NO: 70,493, splice variants which differ in a variant region from an original sequence, and so forth. None of these additional sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim. This is a rejection based on a lack of WRITTEN DESCRIPTION.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled

in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: 70,493; the skilled artisan cannot envision the detailed chemical structure of the encompassed amino acid sequences, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The amino acid sequence itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such

descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." *Id.* at 1170, 25 USPQ2d at 1606.

The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

Therefore, only SEQ ID NO: 70,493 but not the full breadth of claim 3 meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

No claim is allowed.

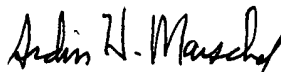
Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703)308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703)308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703)308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703)305-3524 or to the Technical Center receptionist whose telephone number is (703)308-0196.

February 27, 2003

  
ARDIN H. MARSCHEL  
PRIMARY EXAMINER